IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Robert BOIZEL et al.	:	Group Art Unit.: 1609
Serial No.: 10/580,602	:	Examiner: BLAND, Layla D.
Filed: May 25, 2006	:	

Title: USE OF PENTADIENOIC ACID DERIVATIVES FOR THE TREATMENT OF HYPERURICEMIA

APPEAL BRIEF

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Further to the Notice of Appeal filed on March 28, 2008, please consider the following.

The Appeal Brief fee of $ 510.00 is filed/paid herewith.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

(i) REAL PARTY IN INTEREST

The real party in interest is Merck Patent Gmbh, which is recorded at Reel/Frame: 017956/0487.

(ii) RELATED APPEALS AND INTERFERENCES

There are no known related appeals or interferences.

(iii) STATUS OF CLAIMS

Claims 1-19, 23-25 and 34-41 are pending in the present application.

Claims 20-22 and 26-33 were cancelled.

Claims 7, 12 and 34 were withdrawn from consideration.

Claims 1-6, 8-11, 13-19, 23-25 and 35-41 were rejected.

Claims 1-6, 8-11, 13-19, 23-25 and 35-41 are on appeal.

No claims were allowed.

(iv) STATUS OF AMENDMENTS

No amendments were filed after the final rejection.

(v) SUMMARY OF CLAIMED SUBJECT MATTER

Appellants' invention in claim 1 and its dependent claims is directed to a method for preventing or treating hyperuricemia; or for treating a disorder associated with hyperuricemia; or for reducing the serum uric acid level of a subject, which method includes the administration of a compound of formula (I) to a subject who is in need of the claimed methods. See page 1, lines 4-5; page 5, lines 14-33; page 6, lines 3-7; and page 8, line 1 to page 10, line 9.

(vi) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The ground for rejection is the rejections under 35 U.S.C. § 103, i.e., whether claims 1-6, 8-11, 13-19, 23-25 and 35-41 are unpatentable over Brunet et al., WO 00/39113, in view of Chen et al., WO 00/47209.

(vii) ARGUMENT

The Office Action dated December 28, 2007, Office Action hereinafter, admits that WO '113 does not teach the claimed methods, e.g., the indications recited in the method claims are not taught by WO '113. See Office Action page 3, third paragraph.

WO '113 teaches that the compounds of this application are effective for various other indications disclosed therein (see, e.g., page 1, lines 6-9), which indications are not the indications, and do not include the indications, which are the subject of the claimed methods of the present application, because they have the "ability to activate PPARα **and** PPARγ." (Emphasis added.) See page 33, lines 19-21 of WO '113.

WO '209 teaches compounds which are structurally completely different than the compounds of WO '113 (see page 3, second paragraph of WO '209), which compounds are taught to act on PPARγ, which results in the treatment of diseases associated with hyperuricemia (see, e.g., abstract).

Nothing in WO '209 teaches or suggests that the compounds therein having activity on PPARγ only should be replaced with compounds which are dual activators, i.e., compounds which activate PPARα **and** PPARγ, to achieve the treatment of diseases associated with hyperuricemia.

Likewise, nothing in WO '113 suggests that dual activators are useful to treat diseases associated with hyperuricemia or that these compounds could replace single activators in other treatment methods in the art.

Thus, nothing in either reference teaches the interchangeability of these compound types for any reason.

Where the compounds of the two references are structurally completely different, their taught indications are completely different, and their activity profiles are different, i.e., one activates PPARγ, while the other activates PPARα **and** PPARγ, the disclosures of the references are not adequate to teach or suggest to one of ordinary skill in the art the alleged combination thereof for the claimed indications.

Additionally, one of ordinary skill in the art would not have an expectation of success based on what is taught by these references to achieve the claimed invention. See *In re Vaeck*, 947 F.2d, 20 USPQ2d 1438 (CAFC 1991). Nothing in either reference teaches or suggests that compounds which are structurally completely different and have different activity profiles as discussed above should or even could be used interchangeably to achieve a desired result, e.g., the claimed method.

One of ordinary skill in the art reading WO '113 would see that the compounds disclosed therein exhibit hypolipidaemic and hypoglycaemic effects because of their dual activities, i.e., activities on PPARα and PPARγ. Nothing in the prior art provides the expectation to one of ordinary skill in the art that these compounds would retain their usefulness as single activators, e.g., activity only on PPARγ, thereby providing a reasonable doubt on the issue whether the compounds of WO '113 would be effective to treat indications associated with activity only on PPARγ, e.g., leading to treatment of hyperuricemia. Thus, one of ordinary skill in the art would have lacked a reasonable expectation of success in achieving the treatment, e.g., of hyperuricemia with the compounds of WO '113.

Because nothing in either reference teaches or suggests that dual activators of PPARα **and** PPARγ should be used for the treatment of diseases associated with hyperuricemia, one of ordinary skill in the art would not have found a reason to achieve the claimed methods and/or would have lacked a reasonable expectation of success based on the disclosures of

these references. As such, the rejection should be reversed.

Favorable consideration of the patentability of the claimed methods of the present application over the disclosures of WO '113 and WO '209 is respectfully and courteously requested.

Respectfully submitted,

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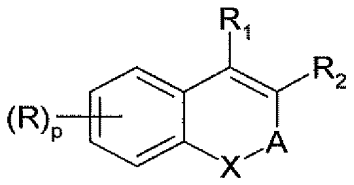
(viii) CLAIMS APPENDIX

1. A method for preventing or treating hyperuricemia; or for treating a disorder associated with hyperuricemia; or for reducing the serum uric acid level of a subject, comprising administering to a subject in need thereof a compound of formula (I)



(I)

in which:

X is O or S;

A is a divalent radical $-(CH_2)_s-CO-(CH_2)_t-$ or $-(CH_2)_s-CR_3R_4-(CH_2)_t-$,

in which s = t = 0 or one of s and t has the value 0 and the other has the value 1;

R_1 and R_2 are, each independently; a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; or a mono- or bicyclic (C_4-C_{12})heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

R_3 and R_4 are, each independently, a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; or a mono- or bicyclic (C_4-C_{12})heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy

group; or

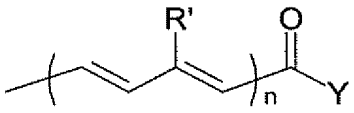
R_3 and R_4 together form a $(C_2$-$C_6)$alkylene chain optionally substituted by a halogen atom or by optionally halogenated $(C_1$-$C_5)$alkoxy;

R is a halogen atom; a cyano group; a nitro group; a carboxy group; an optionally halogenated $(C_1$-$C_{18})$alkoxycarbonyl group; an R_a-CO-NH- or R_aR_bN-CO- group; an optionally halogenated $(C_1$-$C_{18})$alkyl group; optionally halogenated $(C_1$-$C_{18})$alkoxy; and $(C_6$-$C_{10})$aryl, $(C_6$-$C_{10})$aryl$(C_1$-$C_5)$alkyl, $(C_6$-$C_{10})$aryloxy, $(C_3$-$C_{12})$cycloalkyl, $(C_3$-$C_{12})$cycloalkenyl, $(C_3$-$C_{12})$cycloalkyloxy or $(C_3$-$C_{12})$cycloalkenyloxy, in which the aryl, cycloalkyl or cycloalkenyl group is optionally substituted by a halogen atom, by optionally halogenated $(C_1$-$C_5)$alkyl or by an optionally halogenated $(C_1$-$C_5)$alkoxy; -OH;

R_a and R_b are, each independently, an optionally halogenated $(C_1$-$C_{18})$alkyl; a hydrogen atom; $(C_6$-$C_{10})$aryl or $(C_6$-$C_{10})$aryl$(C_1$-$C_5)$alkyl, in which the aryl group is optionally substituted by a halogen atom, by an optionally halogenated $(C_1$-$C_5)$alkyl group or by an optionally halogenated $(C_1$-$C_5)$alkoxy group); $(C_3$-$C_{12})$cycloalkyl optionally substituted by a halogen atom, by an optionally halogenated C_1-C_5 alkyl group or by an optionally halogenated $(C_1$-$C_5)$alkoxy group;

p is 0, 1, 2, 3 or 4;

Z is:



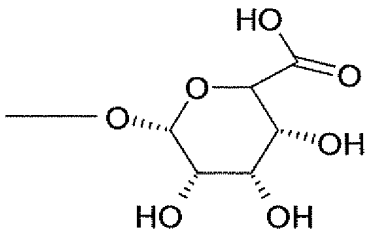
n is 1 or 2;

R' are, each independently, a hydrogen atom; a $(C_1$-$C_5)$alkyl group; a $(C_6$-$C_{10})$aryl group optionally substituted by a halogen atom, by an optionally halogenated $(C_1$-$C_5)$alkyl group or by optionally halogenated $(C_1$-$C_5)$alkoxy; or a mono- or bicyclic $(C_4$-$C_{12})$heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by a

halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

Y is -OH; (C_1-C_5)alkoxy; or -NR_cR_d;

or glucomic acid



R_c and R_d are, each independently, a hydrogen atom; (C_1-C_5)alkyl; (C_3-C_8)cycloalkyl optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy; (C_6-C_{10})aryl optionally substituted by a halogen atom, by optionally halogenated (C_1-C_5)alkyl or by optionally halogenated (C_1-C_5)alkoxy;

wherein one, and one alone, of R_1 and R_2 is Z;

or a pharmaceutically acceptable salt thereof with a acid or base, or an ester thereof.

2. A method according to Claim 1, wherein A is the divalent radical -$(CH_2)_s$-CR_3R_4-$(CH_2)_t$-.

3. A method according to Claim 1,

X is O;

A is -CR_3R_4- or -CH_2-CR_3R_4-, in which the unsubstituted methylene group is bonded to X;

R_1 and R_2 are, each independently, Z; H; (C_1-C_{15})alkyl; (C_2-C_{15})alkenyl; or phenyl

optionally substituted by (C_1-C_5)alkyl, (C_1-C_5)alkoxy, a halogen atom or -CF_3;

R_3 and R_4 are, each independently, a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; or a mono- or bicyclic (C_4-C_{12})heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

R is (C_1-C_9)alkyl; (C_1-C_5)alkoxy; phenyl or phenylcarbonyl optionally substituted by a halogen atom, (C_1-C_5)alkyl, (C_1-C_5)alkoxy, -CF_3 or -OCF_3; a halogen atom; -CF_3 or -OCF_3;

n is 1; and

R' is (C_1-C_5)alkyl or (C_6-C_{10})aryl.

4. A method according to claim 1, wherein

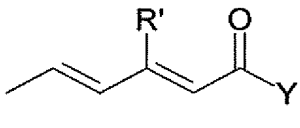
X is O;

A is -CH_2-CR_3R_4-, in which the unsubstituted methylene group is bonded to X;

R_1 and R_2 are, each independently, Z, a hydrogen atom or (C_1-C_5)alkyl;

R_3 and R_4 are, each independently, a hydrogen atom; a (C_1-C_{18})alkyl group; a (C_2-C_{18})alkenyl group; a (C_2-C_{18})alkynyl group; a (C_6-C_{10})aryl group optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group; or a mono- or bicyclic (C_4-C_{12})heteroaryl group containing one or more O, N and/or S atoms, which is optionally substituted by a halogen atom, by an optionally halogenated (C_1-C_5)alkyl group or by an optionally halogenated (C_1-C_5)alkoxy group;

Z is



; and

R' is methyl or phenyl.

5. A method according to claim 1, wherein R_1 is Z.

6. A method according to claim 1, wherein R_2 is a hydrogen atom.

8. A method according to claim 1, wherein

Y is -OH; (C_1-C_5)alkoxy; or -NR_cR_d.

9. A method according to claim 1, wherein R' is methyl.

10. A method according to claim 1, wherein R is (C_1-C_5) alkoxy.

11. A method according to claim 1, wherein p is 0, 1 or 2.

13. A method according to claim 1, wherein the compound of formula (I) is

- (2E, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-6-methoxy-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-[2-(non-6-enyl)-2H-1-benzopyran-3-yl]-3-methylpenta-2,4-dienoic acid;

- (2E, 4E)-5-(4-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(6-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(6-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(4-methyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-undecanyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(5-methyl-2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid; and
- (2E, 4E)-5-(2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7,8-dimethoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydro-7-(para-chlorobenzoyl)benzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

- (2E, 4E)-5-(3,3-dimethyl-7,8-dichloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-bromo-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-fluoro-8-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-fluoro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-trifluoromethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-phenyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3,7-trimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid; or
- (2E, 4E)-5-(9-methoxy-3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

or a pharmaceutically acceptable ester thereof.

14. A method according to claim 1, wherein the disorder associated with hyperuricemia is gout, acute inflammatory arthritis, tophaceous deposition of urate crystals in and around joints, chronic arthritis, deposition of urate crystals in renal parenchyma, urolithiasis, or a related renal disease or gouty nephropathy.

15. A method according to claim 1, wherein the hyperuricemia treated is primary or secondary hyperuricemiae, or the disorder associated with hyperuricemia is hyperuricemiae

related to nephropaties, a myeloproliferative disorder, or a condition associated with insulin resistance or transplantation.

16. A method according to claim 1, wherein the subject has a serum uric acid level, before treatment, equal or above 7 mg/dL (420 μmol/L).

17. A method according to claim 16, wherein gout or a condition brought about by a high level of uric acid in the joints or kidneys or a serum level over 9 mg/dL (530 μmol/L) is treated.

18. A method according to claim 1, wherein the administration is by oral route.

19. A method according to claim 1, wherein the administration is once or twice per day.

23. A method according to claim 1, wherein the amount of a compound of formula (I) administered is 0.15 to 4 mg/Kg of human body weight.

24. A method according to claim 23, wherein said amount is 0.3 to 1.0 mg/Kg human body weight.

25. A method according to claim 1, wherein (2E,4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzo-xepin-5-yl)-3-methylpenta-2,4-dienoic acid, or a pharmaceutically acceptable salt or ester thereof is administered.

35. A method according to claim 1, wherein R_4 is a hydrogen atom or a (C_1-C_{15})alkyl group.

36. A method according to claim 1, wherein a compound of formula I or a pharmaceutically acceptable salt thereof is administered.

37. A method according to claim 1, wherein the compound of formula (I) is

- (2E, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2-pentyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-6-methoxy-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2,2-dimethyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-[2-(non-6-enyl)-2H-1-benzopyran-3-yl]-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(4-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(6-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(6-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-nonyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(4-methyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-undecanyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(2-phenyl-2H-1-benzopyran-3-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(5-methyl-2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid; and

- (2E, 4E)-5-(2,3-dihydrobenzoxepin-4-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-phenylpenta-2,4-dienoic acid;
- (2Z, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7,8-dimethoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydro-7-(para-chlorobenzoyl)benzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7,8-dichloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-bromo-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-fluoro-8-chloro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-fluoro-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-7-trifluoromethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

- (2E, 4E)-5-(3,3-dimethyl-7-phenyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3,7-trimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;
- (2E, 4E)-5-(3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid; or
- (2E, 4E)-5-(9-methoxy-3,3-dimethyl-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid;

or a pharmaceutically acceptable salt thereof.

38. A method according to claim 1, wherein hyperuricemia is prevented.

39. A method according to claim 1, wherein hyperuricemia is treated.

40. A method according to claim 1, wherein a disorder associated with hyperuricemia is treated.

41. A method according to claim 1, wherein serum uric acid level of a subject is reduced.

(ix) EVIDENCE APPENDIX

None

(x) RELATED PROCEEDINGS APPENDIX

None